



SEQUENCE LISTING

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<120> NEUROPROTECTIVE ACTIVITY OF ACTIVATED PROTEIN C  
INDEPENDENT OF ITS ANTICOAGULANT ACTIVITY

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<140> US 10/537,545

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<150> US 60/465,235

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<150> US 60/439,936

<151> 2002-12-05

<160> 1

<170> MS Word

<210> 1

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> peptide

<400> 1

Thr Phe Leu Leu Arg Asn Pro Asn Asp Lys

1

5

10

-continued

ACA	GCG	GCC	CAC	TGC	ATG	GAT	GAG	TCC	AAG	AAG	CTC	CTT	GTC
AGG	CTT	GGA	GAG	TAT	GAC	CTG	CGG	CGC	TGG	GAG	AAG	TGG	GAG
CTG	GAC	CTG	GAC	ATC	AAG	GAG	GTC	TTC	GTC	CAC	CCC	AAC	TAC
AGC	AAG	AGC	ACC	ACC	GAC	AAT	GAC	ATC	GCA	CTG	CTG	CAC	CTG
GCC	CAG	CCC	GCC	ACC	CTC	TCG	CAG	ACC	ATA	GTG	CCC	ATC	TGC
CTC	CCG	GAC	AGC	GGC	CTT	GCA	GAG	CGC	GAG	CTC	AAT	CAG	GCC
GGC	CAG	GAG	ACC	CTC	GTG	ACG	GGC	TGG	GGC	TAC	CAC	AGC	AGC
CGA	GAG	AAG	GAG	GCC	AAG	AGA	AAC	CGC	ACC	TTC	GTC	CTC	AAC
TTC	ATC	AAG	ATT	CCC	GTG	GTC	CCG	CAC	AAT	GAG	TGC	AGC	GAG
GTC	ATG	AGC	AAC	ATG	GTG	TCT	GAG	AAC	ATG	CTG	TGT	GCG	GGC
ATC	CTC	GGG	GAC	CGG	CAG	GAT	GCC	TGC	GAG	GGC	GAC	AGT	GGG
GGG	CCC	ATG	GTC	GCC	TCC	TTC	CAC	GGC	ACC	TGG	TTC	CTG	GTG
GGC	CTG	GTG	AGC	TGG	GGT	GAG	GGC	TGT	GGG	CTC	CTT	CAC	AAC
TAC	GGC	GTT	TAC	ACC	AAA	GTC	AGC	CGC	TAC	CTC	GAC	TGG	ATC
CAT	GGG	CAC	ATC	AGA	GAC	AAG	GAA	GCC	CCC	CAG	AAG	AGC	TGG
GCA	CCT	TAG-3'											

wherein

A is deoxyadenyl,  
G is deoxyguanyl,

R is 5'-GCC CAC CAG GTG CTG CGG ATC  
CGC AAA CGT-3',  
R<sup>1</sup> must necessarily be

5'-ATG	TGG	CAG	CTC	ACA	AGC	CTC	CTG	CTG	TTC	GTG
GCC	ACC	TGG	GGA	ATT	TCC	GGC	ACA	CCA	GCT	CCT
CTT	GAC	TCA	GTG	TTC	TCC	AGC	AGC	GAG	CGT-3'	

C is deoxycytidyl,

T is thymidyl,

R is 5'-GCC CAC CAG GTG CTG CGG ATC  
CGC, AAA CGT-3' or 5'-CAC CAG GTG CTG

and that when

R is 5'-CAC CAG GTG CTG CGG ATC CGC  
AAA CGT-3',  
R<sup>1</sup> must necessarily be

5'-ATG	TGG	CAG	CTC	ACA	AGC	CTC	CTG	CTG	TTC	GTG
GCC	ACC	TGG	GGA	ATT	TCC	GGC	ACA	CCA	GCT	CCT
CTT	GAC	TCA	GTG	TTC	TCC	AGC	AGC	GAG	CGT	GCC-3'

CGG ATC CGC AAA CGT-3'  
R<sup>1</sup> is

The compounds of the present invention encode  
human protein C, and the heretofore unknown amino

5'-ATG	TGG	CAG	CTC	ACA	AGC	CTC	CTG	CTG	TTC	GTG
GCC	ACC	TGG	GGA	ATT	TCC	GGC	ACA	CCA	GCT	CCT
CTT	GAC	TCA	GTG	TTC	TCC	AGC	AGC	GAG	CGT-3'	
or 5'-ATG	TGG	CAG	CTC	ACA	AGC	CTC	CTG	CTG	TTC	GTG
GCC	ACC	TGG	GGA	ATT	TCC	GGC	ACA	CCA	GCT	CCT
CTT	GAC	TCA	GTG	TTC	TCC	AGC	AGC	GAG	CGT	GCC-3'

M is 0 or 1, and  
N is 0 or 1,  
provided that when M is 0, N must necessarily also be 0;  
and that when

acid sequence of nascent human protein C when M and  
N are 1. The amino acid sequence, numbered to facili-  
tate further discussion, of nascent human protein C is:

5 10 15  
H<sub>2</sub>N-MET TRP GLN LEU THR SER LEU LEU PHE VAL ALA THR TRP GLY ILE  
20 25 30  
SER GLY THR PRO ALA PRO LEU ASP SER VAL PHE SER SER GLU ARG  
35 40 45  
ALA HIS GLN VAL LEU ARG ILE ARG LYS ARG ALA ASN SER PHE LEU GLU  
50 55 60  
GLU LEU ARG HIS SER SER LEU GLU ARG GLU CYS ILE GLU GLU ILE CYS  
65 70 75 80  
ASP PHE GLU GLU ALA LYS GLU ILE PHE GLN ASN VAL ASP ASP THR LEU  
85 90 95  
ALA PHE TRP SER LYS HIS VAL ASP GLY ASP GLN CYS LEU VAL LEU PRO  
100 105 110  
LEU GLU HIS PRO CYS ALA SER LEU CYS CYS GLY HIS GLY THR CYS ILE

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      115      120      125
ASP GLY ILE GLY SER PHE SER CYS ASP CYS ARG SER GLY TRP GLU GLY

      130      135      140
ARG PHE CYS GLN ARG GLU VAL SER PHE LEU ASN CYS SER LEU ASP ASN

      145      150      155      160
GLY GLY CYS THR HIS TYR CYS LEU GLU GLU VAL GLY TRP ARG ARG CYS

      165      185      190
SER CYS ALA PRO GLY TYR LYS LEU GLY ASP ASP LEU LEU GLN CYS HIS

      180      185      190
PRO ALA VAL LYS PHE PRO CYS GLY ARG PRO TRP LYS ARG MET GLU LYS

      195      200      205
LYS ARG SER HIS LEU LYS ARG ASP THR GLU ASP GLN GLU ASP GLN VAL

      210      215      220
ASP PRO ARG LEU ILE ASP GLY LYS MET THR ARG ARG GLY ASP SER PRO

      225      230      235      240
TRP GLN VAL VAL LEU LEU ASP SER LYS LYS LYS LEU ALA CYS GLY ALA

      245      250      255
VAL LEU ILE HIS PRO SER TRP VAL LEU THR ALA ALA HIS CYS MET ASP

      260      265      270
GLU SER LYS LYS LEU LEU VAL SRG LEU GLY GLU TYR ASP LEU ARG ARG

      275      280      285
TRP GLU LYS TRP GLU LEU ASP LEU ASP ILE LYS GLU VAL PHE VAL HIS

      290      295      300
PRO ASN TYR SER LYS SER THR THR ASP ASN ASP ILE ALA LEU LEU HIS

      305      310      315      320
LEU ALA GLN PRO ALA THR LEU SER GLN THR ILE VAL PRO ILE CYS LEU

      325      330      335
PRO ASP SER GLY LEU ALA GLU ARG GLU LEU ASN GLN ALA GLY GLN GLU

      340      345      350
THR LEU VAL THR GLY TRP GLY TYR HIS SER SER ARG GLU LYS GLU ALA

      355      360      365
LYS ARG ASN ARG THR PHE VAL LEU ASN PHE ILE LYS ILE PRO VAL VAL

      370      375      380
PRO HIS ASN GLU CYS SER GLU VAL MET SER ASN MET VAL SER GLU ASN

      385      390      395      400
MET LEU CYS ALA GLY ILE LEU GLY ASP ARG GLN ASP ALA CYS GLU GLY

      405      410      415
ASP SER GLY GLY PRO MET VAL ALA SER PHE HIS GLY THR TRP PHE LEU

      420      425      430
VAL GLY LEU VAL SER TRP GLY GLU GLY CYS GLY LEU LEU HIS ASN TYR

      435      440      445
GLY VAL TYR THR LYS VAL SER ARG TYR LEU ASP TRP ILE HIS GLY HIS

      450      455      460
ILE ARG ASP LYS GLU ALA PRO GLN LYS SER TRP ALA PRO-COOH

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wherein

$H_2N$ - is the amino-terminus,  
 -COOH is the carboxy-terminus,  
 ALA is Alanine,  
 ARG is Arginine,  
 ASN is Asparagine,  
 ASP is Aspartic acid,  
 CYS is Cysteine,  
 GLN is Glutamine,  
 GLU is Glutamic Acid,  
 GLY is Glycine,  
 HIS is Histidine,  
 ILE is Isoleucine,

LEU is Leucine,  
 LYS is Lysine,  
 MET is Methionine,  
 PHE is Phenylalanine,  
 60 PRO is Proline,  
 SER is Serine,  
 THR is Threonine,  
 TRP is Tryptophan,  
 TYR is Tyrosine, and  
 65 VAL is Valine.

The DNA compounds of the present invention are derived from cDNA clones prepared from human liver mRNA that encodes human protein C activity. In con-